Claims

1. Peptides according to claim 1, with biological activity against infection by HIV, having the amino acid sequence

Z_1-LE-X_1-IP-X_2-X_3-X_4-P-X_5-X_6-X_7-X_8- X_9-X_{10}-K-X_{11}-X_{12}-X_{13}-X_{14}-X_{15}-Z_2,

wherein

X_1 is a lysine, alanine, or aspartic acid;

X_2 is a cysteine, methionine or isoleucine;

X_3 is a serine, cysteine, lysine or glycine;

X_4 is an isoleucine, alanine, phenylalanine or cysteine;

X_5 is a proline, D-proline or a substituted L-or D-proline;

X_6 is a cysteine or glutamic acid;

X_7 is an amino acid with a hydrophobic or an aromatic side chain or cysteine;

X_8 is an amino acid with a hydrophobic or an aromatic side chain or cysteine;

X_9 is an amino acid with an aromatic side chain;

X_{10} is a glycine, alanine or asparagine;

X_{11} is a proline, aspartic acid, octahydroindolyl-2-carboxylic acid or D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

X_{12} is a phenylalanine, alanine, glycine, glutamic acid or D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

X_{13} is an amino acid with a hydrophobic or an aromatic side chain;

X_{14} is an amino acid with a hydrophobic or an aromatic side chain;

X_{15} is a phenylalanine or deletion;

Z_1 is NH_2 or a sequence of 1 to 10 amino acid residues;

Z_2 is COOH or a sequence of 1 to 10 amino acid residues;

and peptides which are fragments and/or covalently linked oligomers and/or derivatives, especially amidated, alkylated, acylated, sulfated, pegylated, phosphorylated and/or glycosylated derivatives, and mutants thereof;

and with the provisio that

(a) if X_{12} is alanine, glycine, glutamic acid, or D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid than X_{13}, X_{14} and X_{15} are phenylalanine, valine and phenylalanine respectively; and/or

(b) if X_{12} is phenylalanine, than X_{13}, X_{14} and X_{15} are valine, phenylalanine and a deletion, respectively; and

(c) that there are at maximum two cysteine residues in a peptide.

2. Peptides according to claim 1 with a biological activity against infection by HIV having the amino acid sequence

Z_1-LE-X_1-IP-X_1-X_3-X_4-P-X_5-X_6-X_7-X_8- X_9-X_{10}-K-X_{11}-FVF-Z_2;

wherein

X_1 is a lysine, alanine or aspartic acid;

X_2 is a cysteine, methionine or isoleucine;

X_3 is a serine, cysteine or glycine;

X_4 is a isoleucine or cysteine;

X_5 is a proline, D-proline or any substituted L- or D-proline;

X_6 is a cysteine or glutamic acid;

X_7 is a phenylalanine, cysteine, valine, isoleucine or 3,3-diphenylalanine;

X_8 is a phenylalanine, leucine, alanine, glycine, cysteine, D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid or L-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid;

X_9 is an amino acid with an aromatic side chain;

X_{10} is a glycine or asparagine;

X_{11} is a proline or D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic;

Z_1 is NH_2 or a sequence of 1 to 10 amino acid residues;

Z_2 is COOH or a sequence of 1 to 10 amino acid residues;

and peptides which are fragments and/or covalently linked oligomers and/or derivatives, especially amidated, alkylated, acylated, sulfated, pegylated, phosphorylated and/or glycosylated derivatives, and mutants thereof,

with the provisio that

(a) if two cysteine residues are present, said residues are separated by

four other amino acid residues; and

(b) L-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid (L-Tic), D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (D-Tic) and/or 3,3-diphenylalanine are present, no cysteine residue is present.

3. Peptides according to claims 1 to 2 with a biological activity against infection by HIV, having the amino acid sequence
Z_1-LE-X_2-IP-X_2-X_3-IP-X_5-X_6-X_7-X_8-F-X_{10}-KPFVF-Z_2,
wherein
X_1 is a lysine, alanine or aspartic acid;
X_2 is a cysteine, methionine or isoleucine;
X_3 is a serine or glycine;
X_5 is a L-proline, D-proline or any substituted L- or D-proline
X_6 is a cysteine or glutamic acid;
X_7 is a phenyalalnine or valine;
X_8 is a phenylalanine, leucine, alanine or L-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid;
X_{10} is a glycine or asparagine;
Z_1 is NH_2 or a sequence of 1 to 10 amino acid residues;
Z_2 is COOH or a sequence of 1 to 10 amino acid residues, and
and peptides which are fragments and/or covalently linked oligomers and/or derivatives, especially amidated, alkylated, acylated, sulfated, pegylated, phosphorylated and/or glycosylated derivatives, and mutants thereof.

4. Peptides according to claim 1 to 3, having the amino acid sequence
Z_1-LEAIP-X_2-SIP-X_5-X_6-V-X_8-FNKPFVF-Z_2,
wherein
X_2 and X_6 are cysteines, or X_2 is methionine and X_6 is glutamic acid
X_5 is a D-proline or L-proline;
X_8 is an amino acid with a hydrophobic or an aromatic side chain or lysine;
Z_1 is NH_2 or a sequence of 1 to 10 amino acid residues;

Z_2 is COOH or a sequence of 1 to 10 amino acid residues;
and peptides which are fragments and/or covalently linked oligomers and/or derivatives, especially amidated, alkylated, acylated, sulfated, pegylated, phosphorylated and/or glycosylated derivatives, and mutants thereof, with biological activity against infection by HIV,
with the proviso that at least one of the following is true:
X_2 is D-proline or
X_5 is not lysine or
X_6 and X_8 are cysteine.

5. Peptides according to anyone of the claim 1 to 4, wherein the cysteine residues at positions 6 and 11, 6 and 12, 7 and 12, or 8 and 13 are connected by an intramolecular disulfide bond.

6. Peptides according to anyone of the claim 1 to 4, with a single cysteine residue, wherein said cysteine residue is connected by an intermolecular disulfide bond to another peptide with a single cysteine residue, forming a homo-dimer.

7. Peptides according to anyone of the claims 1 to 6, wherein the leucine residue at amino acid position 1 and the glutamic acid at amino acid position 2 are covalently linked by an N-alkylated amide bond or by an ester bond or by a reduced peptide bond or by a retro-inverso peptide bond or by an N-alkylated retro-inverso peptide bond.

8. Peptides according to any of the claims 1 to 7 with one of the amino acid sequences

VIR-121	LEAIPMSIPpEVAFNKPFVF	SEQ ID NO. 2
VIR-161	LEAIPCSIPpCVAFNKPFVF	SEQ ID NO. 3
VIR-162	LEAIPCSIPPCVGFGKPFVF	SEQ ID NO. 4
VIR-163	LEAIPCSIPPCVLFNKPFVF	SEQ ID NO. 5

VIR-164	LEAIPCSIPPCVFFNKPFVF	SEQ ID NO. 6
VIR-165	LEAIPCSIPPCFAFNKPFVF	SEQ ID NO. 7
VIR-166	LEAIPCSIPPCVA(D-Tic)NKP(D-Tic)FVF	SEQ ID NO. 8
VIR-170	LEAIPMSIPPEVFFGKPFVF	SEQ ID NO. 9
VIR-175	LEAIPMSIPPEFLFGKPFVF	SEQ ID NO. 10
VIR-182	LEAIPMSIPPELAFAKPFVF	SEQ ID NO. 11
VIR-184	LEAIPMSIPPEIAFNKPFVF	SEQ ID NO. 12
VIR-190	LEAIPMSIPpEVGFGKPFVF	SEQ ID NO. 13
VIR-191	LEAIPMSIPpEVLFGKPFVF	SEQ ID NO. 14
VIR-192	LEAIPMSIPpEVFFGKPFVF	SEQ ID NO. 15
VIR-193	LEAIPMSIPpEFAFNKPFVF	SEQ ID NO. 16
VIR-197	LEAIPMSIPpEVFFNKPFVF	SEQ ID NO. 17
VIR-199	LEAIPMSIPpEFLFNKPFVF	SEQ ID NO. 18
VIR-229	LEAIPISIPpEVAFNKPFVF	SEQ ID NO. 19
VIR-234	LEAIPMGIPpEVAFNKPFVF	SEQ ID NO. 20
VIR-243	LEAIPMSIPPEFAFNKDFVF	SEQ ID NO. 21
VIR-252	LEDIPMSIPpEVAFNKPFVF	SEQ ID NO. 22
VIR-255	LEKIPMSIPpEVAFNKPFVF	SEQ ID NO. 23
VIR-257	LEAIPMSIPpEV(cyclohexylalanine)FNKPFVF	SEQ ID NO. 24
VIR-258	LEAIPMSIPpE(1-naphthylalanine)AFNKPFVF	SEQ ID NO. 25
VIR-259	LEAIPMSIPpE(p-fluorophenylanine)AFNKPFVF	SEQ ID NO. 26
VIR-260	LEAIPMSIPpEV(4-pyridylalanine)FNKPFVF	SEQ ID NO. 27
VIR-261	LEAIPMSIPpE(3,3-diphenylalanine)AFNKPFVF	SEQ ID NO. 28
VIR-262	LEAIPMSIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 29
VIR-263	LEAIPMSIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 30
VIR-264	LEAIPMSIPpEV(3-benzothienylalanine)FNKPFVF	SEQ ID NO. 31
VIR-265	LEAIPMSIPpEV(3-thienylalanine)FNKPFVF	SEQ ID NO. 32
VIR-266	LEAIPMSIPpEVWFNKPFVF	SEQ ID NO. 33
VIR-268	LEAIPMSIPpEVAFNK(L-Tic)FVF	SEQ ID NO. 34
VIR-269	LEAIPMSIPpEVAFNK(Oic)FVF	SEQ ID NO. 35
VIR-272	LEAIPMCIPPECLFNKPFVF	SEQ ID NO. 36
VIR-273	LEAIPMCIPPECFFNKPFVF	SEQ ID NO. 37

VIR-274	LEAIPMCIPPECLFGKPFVF	SEQ ID NO. 38
VIR-280	LEAIPCSIPPCFLFGKPFVF	SEQ ID NO. 39
VIR-284	LEAIPISIPPEVFFGKPFVF	SEQ ID NO. 40
VIR-286	LEAIPISIPPELAFAKPFVF	SEQ ID NO. 41
VIR-290	LEAIPISIPpEVFFGKPFVF	SEQ ID NO. 42
VIR-298	LEAIPISIPpEVWFNKPFVF	SEQ ID NO. 43
VIR-320	LEAIPMGIPpEVFFGKPFVF	SEQ ID NO. 44
VIR-322	LEAIPMGIPpEVFFNKPFVF	SEQ ID NO. 45
VIR-323	LEAIPMGIPpEFLFNKPFVF	SEQ ID NO. 46
VIR-326	LEDIPMGIPpEVAFNKPFVF	SEQ ID NO. 47
VIR-328	LEAIPMGIPpEVWFNKPFVF	SEQ ID NO. 48
VIR-344	LEAIPCSIPPCVFFGKPFVF	SEQ ID NO. 49
VIR-345	LEAIPCSIPPCFLFGKPFVF	SEQ ID NO. 50
VIR-346	LEAIPCSIPPCLAFAKPFVF	SEQ ID NO. 51
VIR-348	LEAIPCSIPpCVGFGKPFVF	SEQ ID NO. 52
VIR-350	LEAIPCSIPpCVFFGKPFVF	SEQ ID NO. 53
VIR-351	LEAIPCSIPpCFAFNKPFVF	SEQ ID NO. 54
VIR-352	LEAIPCSIPpCVFFNKPFVF	SEQ ID NO. 55
VIR-353	LEAIPCSIPpCFLFNKPFVF	SEQ ID NO. 56
VIR-354	LEAIPCSIPpCVAFNKPFVF	SEQ ID NO. 57
VIR-355	LEAIPCGIPpCVAFNKPFVF	SEQ ID NO. 58
VIR-356	LEAIPCSIPPCFAFNKDFVF	SEQ ID NO. 59
VIR-357	LEDIPCSIPpCVAFNKPFVF	SEQ ID NO. 60
VIR-358	LEKIPCSIPpCVAFNKPFVF	SEQ ID NO. 61
VIR-376	LEAIPMSIPpEFLFGKPAFVF	SEQ ID NO. 62
VIR-377	LEAIPMSIPpEFLFGKPGFVF	SEQ ID NO. 63
VIR-380	LEAIPMSIPpEFLFGKPFFVF	SEQ ID NO. 64
VIR-384	LEAIPMSIPpEFLFGKPEFVF	SEQ ID NO. 65
VIR-396	LEAIPMSAPpEFLFGKPFVF	SEQ ID NO. 66
VIR-400	LEAIPMSFPpEFLFGKPFVF	SEQ ID NO. 67
VIR-416	LEAIPMGIPpEFLFGKPFVF	SEQ ID NO. 68
VIR-418	LEKIPMGIPpEFLFGKPFVF	SEQ ID NO. 69

VIR-445	LEAIPISIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 70
VIR-447	LEAIPISIPpEVAFNK(L-Tic)FVF	SEQ ID NO. 71
VIR-448	LEAIPMGIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 72
VIR-449	LEAIPMGIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 73
VIR-452	LEDIPMSIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 74
VIR-454	LEKIPMSIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 75
VIR-455	LEKIPMSIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 76
VIR-479	LEDIPIGIPpEFLFNKPFVF	SEQ ID NO. 77
VIR-483	LEKIPIGIPpEV(D-Tic)FNKPFVF	SEQ ID NO. 78
VIR-484	LEKIPIGIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 79
VIR-485	LEKIPIGIPpEVAFNK(L-Tic)FVF	SEQ ID NO. 80
VIR-487	LEDIPIGIPpEV(L-Tic)FNKPFVF	SEQ ID NO. 81
VIR-488	LEDIPIGIPpEVAFNK(L-Tic)FVF	SEQ ID NO. 82
VIR-512	*N-Me*-LEAIPMSIPPEFLFGKPFVF	SEQ ID NO. 83
VIR-568	LEAIPMSCPPEFCFGKPFVF	SEQ ID NO. 84
VIR-570	LEAIPCSIPPECLFGKPFVF	SEQ ID NO. 85
VIR-576	$(LEAIPCSIPPEFLFGKPFVF)_2$	SEQ ID NO. 86
VIR-580	LEAIPMSIPPEFLFGKPFVF-miniPEG	SEQ ID NO. 87
VIR-590	LEAIPMKIPPEFLFGKPFVF	SEQ ID NO. 88

9. The peptides according to anyone of claims 1 to 8, which interact with the fusion peptide of HIV.

10. The peptides according to anyone of claims 1 to 9, which have an IC_{50} of equal or below 6500 nM, preferably those having an IC_{50} of equal or below 2000 nM and most preferably those having an IC_{50} of equal or below 800 nM such as VIR-344 (SEQ ID NO. 49) with an IC_{50} of 348 nM, VIR-345 (SEQ ID NO. 50) with an IC_{50} of 298 nM, VIR-353 (SEQ ID NO. 56) with an IC_{50} of 225 nM, VIR-357 (SEQ ID NO. 60) with an IC_{50} of 497 nM, VIR-358 (SEQ ID NO. 61) with an IC_{50} of 706 nM, VIR-449 (SEQ ID NO. 73) with an IC_{50} of 274 nM, VIR-455 (SEQ ID NO. 76) with an IC_{50} of 134 nM, VIR-484 (SEQ ID NO. 79) with an IC_{50} of 100 nM, VIR-512 (SEQ ID NO. 83) with an

IC_{50} of 138 nM, VIR-576 (SEQ ID NO. 86) with an IC_{50} of 107 nM and VIR-580 (SEQ ID NO. 87) with an IC_{50} of 150 nM.

11. Nucleic acids coding for peptides according to any of claims 1 to 10.

12. Antibodies binding specifically to peptides according to claims 1 to 10.

13. A medicament containing the peptides according to claims 1 to 10, nucleic acids of claim 11 or antibodies of claim 12.

14. The medicament of claim 13 in galenic formulations for oral, intravenous, intramuscular, intracutaneous, subcutaneous, intrathecal administration, and as an aerosol for transpulmonary administration.

15. The medicament of claim 13 or 14 comprising at least one further therapeutic agent.

16. The medicament of claim 15, wherein the said at least one further therapeutic agent is a viral protease inhibitor, a reverse transcriptase inhibitor, a fusion inhibitor, a cytokine, a cytokine inhibitor, a glycosylation inhibitor or a viral mRNA inhibitor.

17. Use of the peptides according to claims 1 to 10 for the manufacturing of a medicament for the treatment of HIV infections.

18. An assay for determining molecules capable of interaction with the fusion peptide of HIV, comprising a peptide according to anyone of claims 1 to 10.

19. Use of the peptides according to anyone of claims 1 to 10 in an assay according to claim 16.

20. A diagnostic agent containing peptides according to any of claims 1 to 10, nucleic acids according to claim 11 or antibodies according to claim 12.

21. Use of the diagnostic agent according to claim 18 for assay systems for testing isolated plasma, tissue, urine and cerebrospinal fluid levels for HIV infection.